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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER
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ART UNIT	PAPER NUMBER
1635	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/937,643	Applicant(s) PHILLIPS ET AL.	
	Examiner J. Eric Angell	Art Unit 1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 July 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *26-56* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *26-56* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

This action is in response to the amendment filed 7/29/02 as Paper No. 11. As mentioned in the previous Office Action, claims added as new claims 32-65 in the communication filed 3/20/02 were renumbered in accordance with 37 CFR 1.126 as claims **26-59.** Claims 26-50 have been amended and claims 57-59 have been cancelled, as set forth in the amendment filed 7/29/02. It is noted that Applicants state in the amendment filed 7/29/02, "Please cancel claims 57-65. Please amend claims 32-56 as follows" (see page 2 of the 7/29/02 communication). However, only claims 26-59 were pending in the application, therefore only claims 57-59 could be cancelled as claims 60-65 are not present in the application. Furthermore, Applicants amended claims 26-50 (see pgs 2-5 of the 7/29/02 communication), therefore claims 26-50 were amended, but claims 51-56 have not amended and have not cancelled. Claims 26-58 are pending in the application and addressed herein.

Claim Rejections - 35 USC § 102

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

2. Claims 26-35, 38-47, and 49-56 are rejected under 35 U.S.C. 102(b) as being anticipated by Morales et al. (J. Urology 153:1706-1710; 1995).Morales teaches a method of treating prostate cancer comprising administration of a composition comprising mycobacterial DNA (B-DNA) from M. phlei (see p. 1706, first column) and a pharmaceutically acceptable carrier (such

as oil microdroplets; p. 1706 first column) to an animal having prostate cancer in an amount effective to have an antineoplastic effect (i.e. inhibition of proliferation of cancer cells) on prostate cancer in the animal having the cancer (see abstract, Fig. 2); wherein the pharmaceutical acceptable carrier is M. phlei cell wall (p. 1706, first column), the M. phlei DNA is preserved and complexed to the cell wall (note the cell wall would inherently have the cell's DNA preserved and complexed to the cell wall unless the cell wall was specifically treated to remove the DNA with agents such as nucleases), and wherein the prostate cancer contains hormone sensitive cells (e.g. androgens such as testosterone) (see p.1706, first column).

Response to Arguments

3. Applicant's arguments filed 7/29/02 have been fully considered but they are not persuasive.

Applicants argue that Morales does not teach each and every element of the invention as arranged in the claims. Applicants contend that Morales does not teach a method for treating prostate cancer comprising administration of a composition comprising mycobacterial DNA in a pharmaceutically acceptable carrier, wherein the pharmaceutically acceptable carrier is mycobacterial cell wall. Applicants also contend that Morales does not teach the use of M. phlei DNA or the use of M. phlei DNA cell wall complex. Applicants state that pending claims 51-59, drawn to mycobacterial cell walls and a pharmaceutically acceptable carrier, have been cancelled. Applicants also argue that Morales does not teach M. phlei cell walls can be used as pharmaceutically acceptable carriers for M. phlei DNA. Applicants contend that the M. phlei

cell wall complex of Morales would not inherently have M. phlei DNA preserved and complexed to the MCW, and that Morales does not disclose the use of M. phlei DNA.

In response, it is respectfully pointed out that Morales states "We now report the antineoplastic activity of MCW on the R3327-H variant of the Dunning rat adenocarcinoma of the prostrate." (See p. 1706, second column). Morales defines MCW as M. phlei cell wall (see page 1706, first column). Therefore, Morales teaches that M. phlei cell wall complex has anti-tumor effects on prostate tumor cells. Morale indicates that the "all animals initially received 1 intratumoral injection of 1000 μg MCW emulsion" (see p. 1706 under "Treatment") thus indicating that the MCW can be a pharmaceutically acceptable carrier. The MCW taught by Morales would inherently contain M. phlei DNA, as evidenced by Filion (Blood 90(10), Supp. 1:58B). Filion indicates, "Regressin, an emulsion containing a mycobacterial cell wall complex (MCC) derived from M. phlei, has been shown to have potent anti-tumor activity... Examination of M. phlei MCC using molecular biological techniques has shown that it contains genomic DNA and a range of lower molecular weight DNA oligonucleotides... In conclusion, our results show that M. phlei DNA is able to induce IL-12 synthesis in monocytes and macrophages and that it contributes significantly to the overall activity of M. phlei MCC" (see Filion, Blood 90(10), abstract 2959). Therefore, M. phlei cell wall complex contains M. phlei DNA, which contributes to the anti-tumoral effect of the mycobacterial cell wall complex. Applicants admit in the response filed 7/29/02 that "It is possible that the M. phlei cell walls used in the Morales study contained DNA", but applicants also argue, "it is also possible the cell walls were treated with nucleases" (see p. 8 of response filed 7/29/02). It is noted that Attorney argument is not evidence unless it is an admission, in which case, an examiner may use the admission in making

a rejection. See MPEP § 2129 and § 2144.03 for a discussion of admissions as prior art.

Furthermore, MPEP 2145 states:

> "The arguments of counsel cannot take the place of evidence in the record. In re Schulze, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965); In re Geisler, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997) ("An assertion of what seems to follow from common experience is just attorney argument and not the kind of factual evidence that is required to rebut a prima facie case of obviousness."). See MPEP § 716.01(c) for examples of attorney statements which are not evidence and which must be supported by an appropriate affidavit or declaration."

Here, the M. phlei cell wall complex used by Morales is identical, or substantially identical to the composition of M. phlei cell wall complex used by Filion. Regarding identical or substantially identical compositions, MPEP 2112.01 states:

> "Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a prima facie case of either anticipation or obviousness has been established. In re Best, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). 'When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not.' In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). Therefore, the prima facie case can be rebutted by evidence showing that the prior art products do not necessarily possess the characteristics of the claimed product."

Therefore, the M. phlei MCW of Morales would inherently have the M. phlei DNA complexed to the mycobacterial cell wall, as there is no indication that the DNA of Morales' MCW has been degraded or removed. As mentioned above, without any indication that the DNA was removed, the MCW used by Morales would inherently comprise M. phlei DNA.

Claim Rejections - 35 USC § 103

4. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

5. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 26-59 are rejected under 35 U.S.C. 103(a) as being unpatentable over Morales et al. (J. Urology 153:1706-1710; 1995) in view of Filion et al. (Blood 90(10), Suppl.1:p.58B; 1997).

Morales teaches a method of treating prostate cancer comprising administration of a composition comprising mycobacterial DNA (B-DNA) from M. phlei (see p. 1706, first column) and a pharmaceutically acceptable carrier (such as oil microdroplets; p. 1706 first column) to an animal having prostate cancer in an amount effective to have an antineoplastic effect (i.e. inhibition of proliferation of cancer cells) on prostate cancer in the animal having the cancer (see abstract, Fig. 2); wherein the pharmaceutical acceptable carrier is M. phlei cell wall (p. 1706, first column), the M. phlei DNA is preserved and complexed to the cell wall (note the cell wall

would inherently have the cell's DNA preserved and complexed to the cell wall unless the cell wall was specifically treated to remove the DNA with agents such as nucleases), and wherein the prostate cancer contains hormone sensitive cells (e.g. androgens such as testosterone) (see p.1706, first column).

Morales does not teach that the administration comprises administration of an immunological agent or that the antineoplastic effect is induction of a cytokine, such as IL-12.

Filion teaches that M. phlei cell wall complex is an antitumoral agent that induces IL-12 synthesis when injected into mice (p. 58B).

It would have been prima facie obvious to one having ordinary skill in the art at the time the invention was made to utilize the method of Morales to induce IL-12 production in animals with prostate cancer since Filion teaches that M. phlei cell wall complex can induce IL-12 synthesis, and thus is an immunological agent. An ordinary artisan would have been motivated to combine these references to create a method where M. phlei complexed cell wall is used to treat prostate cancer by inducing IL-12 production since Filion states, "IL-12 synthesized in response to this DNA [M. phlei DNA] may be in part responsible for the antitumor activity of M. phlei MCC (Regressin)." (see last line, p. 58B).

Response to Arguments

7. Applicant's arguments filed 7/29/02 have been fully considered but they are not persuasive.

Applicants contend that the claimed invention does not recite the use of mycobacterial cell walls for treating any disease. Applicants argue that Morales teaches a method of treating

prostate cancer, while Filion teaches treating other forms of cancer and therefore it would not have been obvious to combine the methods to treat prostate cancer. Applicants also argue that Morales does not disclose the use of DNA for treating prostate cancer, and asserts that the claimed invention recites the use of mycobacterial DNA which includes specific amounts of DNA. Applicants also argue that neither Filion nor Morales teaches a composition that may be used to treat androgen sensitive and androgen insensitive prostate cancer cells.

In response, it is respectfully pointed out that the claims 51-57 have not been cancelled, therefore the claimed invention does recite the use of mycobacterial cell walls for treating cancer (see claims 51-57). Additionally claims 29-32 indicate that the therapeutic composition comprises mycobacterial cell walls, thus indicating that MCW is used in the treatment of disease. It is acknowledged that Morales does teach a method for treating prostate cancer, while Filion does not expressly state that mycobacterial DNA/cell wall complex can be used to treat prostate cancer. However, Filion indicates that M. phlei DNA does contribute significantly to the overall activity of M. phlei mycobacterial cell wall complex, and that this DNA may be in part responsible for the anti-tumor activity of M. phlei MCC. Therefore, Filion teaches that the M. phlei MCC has anti-tumor activity, indicating that the M. phlei cell wall complex has effects on tumorous cancers, not just non-tumorous cancers such as leukemia as asserted by Applicants (see p. 9, first paragraph of response). Therefore it is reasonable that one of ordinary skill in the art would have been motivated to combine the teachings of Morales and Filion to create a method to treat prostate cancer as Filion indicates that MCC has anti-tumoral activity and Morales teaches a method for treating prostate cancer. Furthermore, the compositions used by Morales and Filion

are identical or substantially identical, as both comprise M. phlei cell wall complex comprising M. phlei DNA, as mentioned above.

In response to the argument that the claimed invention recites the use of mycobacterial DNA or the use of mycobacterial cell wall complex, which includes specific amounts of DNA. It is respectfully pointed out that applicants are arguing elements not present in the claims. Specifically, the claims do not teach specific amounts of mycobacterial DNA used in the treatment or the amount of mycobacterial DNA required for causing antineoplastic activity.

In response to applicants argument that neither Filion nor Morales teaches a composition that may be used to treat androgen sensitive and androgen insensitive prostate cancer cells, it is respectfully pointed out that Morales teaches that M. phlei mycobacterial cell wall (MCW) was used to treat tumors comprising a mixed population of androgen-sensitive and androgen-insensitive malignant cells. Morales teaches that the M. phlei MCW treatment resulted in tumor regression in these mixed cell tumors, indicating that the M. phlei MCW can treat both androgen sensitive and insensitive tumors. Specifically, Morales teaches, "By day 50, treated animals exhibited ulcerative necrosis of the tumor with a continuous decrease in its size (Fig. 3). In 50% of the animals there was a complete tumor regression by day 60, with only a small, scared hairless area of skin remaining at the site of the tumor (Fig. 4)." (see p. 1707, paragraph bridging columns 1-2). The complete remission of the mixed cell tumors indicates that the treatment can treat both androgen-sensitive and androgen-insensitive tumors.

Conclusion

No claim is allowed.

8. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to J. Eric Angell whose telephone number is (703) 605-1165. The examiner can normally be reached on M-F (8:00-4:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader can be reached on (703) 308-0447. The fax phone numbers for

the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

J. Eric Angell
October 16, 2002

JEFFREY FREDMAN
PRIMARY EXAMINER